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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 7/48

A1

(11) International Publication Number: WO 95/23587

(43) International Publication Date: 8 September 1995 (08.09.95)

(21) International Application Number: PCT/US95/02489

(22) International Filing Date: 27 February 1995 (27.02.95)

(30) Priority Data:
08/205,966 3 March 1994 (03.03.94) US

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(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: ANTI-ACNE COMPOSITIONS

(57) Abstract

The subject invention relates to anti-acne compositions comprising a combination of benzoyl peroxide and certain zwitterionic surfactants. The subject invention further relates to methods of treating acne in mammalian skin.

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ANTI-ACNE COMPOSITIONS

TECHNICAL FIELD

The subject invention relates to the field of treatment of acne in mammalian skin. Specifically, the subject invention relates to methods for treatment of acne in human skin.

BACKGROUND OF THE INVENTION

Acne is a pilosebaceous disease characterized by comedo, papules, inflamed nodules and superficial pus-filled cysts. The course and severity of acne is determined by the interaction between hormones, keratinization, sebum formation and bacteria. Acne usually begins at puberty, when the pilosebaceous glands increase in size, and sebum synthetic activity is elevated due to increased circulating levels of androgens. Follicular hyperkeratosis can also occur, causing restriction of pilosebaceous follicles and, consequently, comedo or plug formation. The comedo contains sebum, protein debris, and anaerobic microorganisms including Propionibacterium (Corynebacterium) acnes (P. acnes). P. acnes thrive on sebum and generate inflammatory free fatty acids (FFA). The FFA cause irritation in the follicular wall and can lead to rupture of the follicular wall, inducing an inflamed lesion. In severe cases, this lesion will heal with scarring.

Existing treatments for acne include general topical application of lotions and salves to affected skin areas, as well as localized (spot) topical treatment. Products used for such treatments include anti-bacterial agents, such as benzoyl peroxide.

It is an object of the subject invention to provide topical compositions for the treatment of acne in mammalian skin.

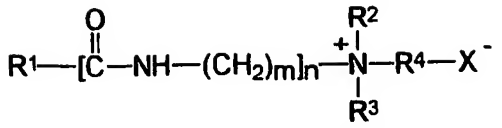
It is a further object of the subject invention to provide such compositions which disrupt the follicular plug, permitting greater delivery of benzoyl peroxide to P. acnes present in the comedone than existing compositions.

It is also an object of the subject invention to provide methods for treatment of acne in mammalian skin.

It is also an object of the subject invention to provide methods for the treatment of acne in mammalian skin which control P. acnes growth by enhancing delivery of benzoyl peroxide.

SUMMARY OF THE INVENTION

The subject invention involves a combination of benzoyl peroxide and certain zwitterionic surfactants having the structure:



wherein

(a) R^1 is unsubstituted, saturated or unsaturated, straight or branched chain alkyl having from about 9 to about 22 carbon atoms;

(b) m is an integer from 1 to 3;

(c) n is 0 or 1;

(d) R^2 and R^3 are, independently, saturated, straight chain alkyl having from 1 to about 3 carbon atoms, unsubstituted or mono-substituted with hydroxy;

(e) R^4 is saturated or unsaturated, straight or branched chain alkyl, which is unsubstituted or mono-substituted with hydroxy, having from 1 to about 5 carbon atoms; and

(f) X is CO_2, SO_3 or SO_4.

The compositions of the subject invention comprise a safe and effective amount of benzoyl peroxide in combination with a safe and effective amount of certain zwitterionic surfactants, and a pharmaceutically-acceptable carrier. The subject invention also includes methods of using such compositions for prevention or treatment of acne.

These and other features, aspects and advantages of the subject invention will become better understood with reference to the following description and appended claims.

DETAILED DESCRIPTION OF THE INVENTION

It has been found that a combination of benzoyl peroxide and certain zwitterionic surfactants are unexpectedly useful in the treatment of acne. While not limited to any specific mechanism, it is believed that the subject compositions exhibit the ability to disrupt the follicular plug in mammalian comedones. It is believed that the subject combination works by affecting the skin surface's proteolytic enzyme which degrades the protein connections (desmosomes) between cells in the follicular plug, thus causing cell or scale shedding.

As used herein "desquamation" means the shedding or removal of scales from the outermost layer (stratum corneum) of the epidermis. Desquamation is believed to aid in the treatment of acne because it disrupts the comedone in skin with acne.

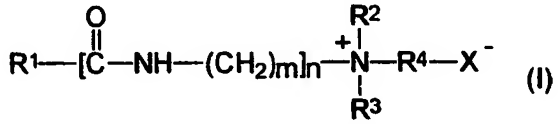
As used herein "treating acne" means preventing, retarding and/or

arresting the process of acne formation in mammalian skin.

As used herein, the term "alkyl", unless otherwise indicated, means carbon-containing chains which may be straight or branched, substituted or unsubstituted, saturated, monounsaturated (i.e. one double bond or triple bond in the carbon chain), or polyunsaturated (i.e. two or more double bonds in the carbon chain, two or more triple bonds in the carbon chain, one or more double and one or more triple bonds in the carbon chain). Preferred alkyl are straight chain. Preferred alkyl are mono- or di-substituted, or unsubstituted, more preferably unsubstituted. Preferred alkyl are saturated or mono-unsaturated and, if so, preferably with a double bond; more preferably, alkyl are saturated.

Preferred alkyl substituents include halogen, aryl, amino, hydroxy, alkoxy, cyano, nitro and trifluoromethyl. More preferred alkyl substituents are halogen and aryl.

As used herein "zwitterionic surfactant" means a compound having the structure:



(I)

In structure (I) R^1 is unsubstituted alkyl having from about 9 to about 22 carbon atoms. Preferred R^1 has from about 11 to about 18 carbon atoms; more preferably from about 12 to about 16 carbon atoms; more preferably still from about 14 to about 16 carbon atoms.

In structure (I), m is an integer from 1 to 3, preferably 2 or 3; more preferably 3.

In structure (I), n is either 0 or 1; n is preferably 1.

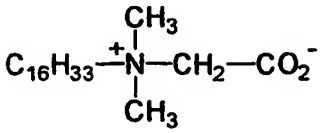
In structure (I), R^2 and R^3 are, independently, selected from the group consisting of saturated, straight chain alkyl having from 1 to about 3 carbon atoms, unsubstituted or mono-substituted with hydroxy. Preferred R^2 and R^3 are CH_3, CH_2CH_2OH, and $CH_2CH_2CH_2OH$. More preferred R^2 and R^3 are CH_3.

In structure (I), X is selected from the group consisting of CO_2, SO_3 and SO_4.

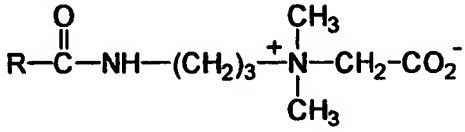
In structure (I), R^4 is alkyl unsubstituted or mono-substituted with hydroxy, having from 1 to about 5 carbon atoms. When X is CO_2, R^4 preferably has 1 or 3 carbon atoms, more preferably 1 carbon atom. When X is SO_3 or SO_4, R^4 preferably has from about 2 to about 4 carbon atoms, more preferably 3 carbon atoms.

Preferred zwitterionic surfactants of the subject invention include the following compounds:

a) cetyl betaine:

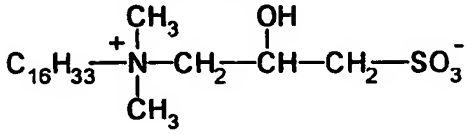


b) cocoamidopropylbetaine:

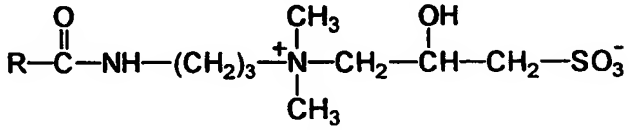


wherein R is unsubstituted, saturated, stright chained alkyl with from about 9 to about 13 carbon atoms;

c) cetyl propyl hydroxy sultaine:

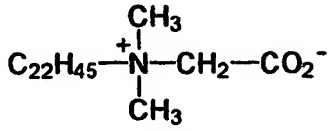


d) cocoamidopropyl hydroxy sultaine:



wherein R is unsubstituted, saturated, straight chained alkyl with from about 9 to about 13 carbon atoms; and

e) behenyl betaine:



More preferred zwitterionic surfactants of the subject invention include cetyl betaine, cocoamidopropyl betaine and cetyl propyl hydroxy sultaine. Still more preferred zwitterionic surfactants of the subject invention include cetyl betaine and cetyl propyl hydroxy sultaine. The most preferred zwitterionic surfactant of the subject invention is cetyl betaine.

As used herein "topical application" means directly laying on or spreading on outer skin.

As used herein, "safe and effective amount" means a sufficient amount of a composition to significantly induce a positive modification in the condition being treated, but low enough to avoid serious side effects.

As used herein "comprising" means that other steps and ingredients which do not affect the end result can be added. This term encompasses the terms "consisting of" and "consisting essentially of".

As used herein, "pharmaceutically-acceptable" means that drugs, medicaments or inert ingredients which the term describes are suitable for use in contact with the tissues of humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response and the like.

As used herein, "actives" or "active agents" means a combination of benzoyl peroxide, and a zwitterionic surfactant according to structure (I) or a mixture of such surfactants.

Compositions useful for treating acne preferably comprise from about 0.1% to about 10%, more preferably from about 1% to about 6%, also preferably about 2% to about 5% of benzoyl peroxide.

Compositions useful for treating acne also preferably comprise from about 0.1% to about 10%, more preferably from about 1% to about 6%, also preferably from about 2% to about 5% of zwitterionic surfactant according to structure (I) or a pharmaceutically-acceptable salt thereof. Preferred pharmaceutically-acceptable salts include alkali metal salts, such as sodium and potassium; alkaline earth metal salts, such as calcium and magnesium; non-toxic heavy metal salts; ammonium salts; and trialkylammonium salts, such as trimethylammonium and triethylammonium.

Pharmaceutically-Acceptable Carrier

In addition to the active agents as described hereinbefore, the pharmaceutical compositions of the present invention essentially comprise a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier", as used herein, means one or more compatible solid or liquid filler diluents which are suitable for administration to a human or lower animal. The term "compatible", as used herein, means that the components of the pharmaceutical compositions are capable of being comingled with the compound of the present invention, and with each other, in a manner such that there is no interaction which would substantially reduce the pharmaceutical efficacy of the pharmaceutical composition under ordinary use situations. Pharmaceutically-acceptable carriers must, of course, be of sufficiently high purity and sufficiently low toxicity to render them suitable for administration to the human or lower

animal being treated.

The compositions of the subject invention are administered topically to a biological subject, i.e., by the direct laying on or spreading of the composition on the skin of the subject. The topical compositions useful in the subject invention involve compositions suitable for topical application to mammalian skin, the composition comprising a safe and effective amount of the active agents or mixture of such actives as described hereinafter, and a pharmaceutically-acceptable topical carrier.

The topical compositions useful in the subject invention may be made into a wide variety of product types. These include, but are not limited to, lotions, creams, gels, sticks, sprays, ointments, pastes, mousses and cosmetics. These product types may comprise several types of carrier systems including, but not limited to solutions, emulsions, gels, solids, and liposomes.

The topical compositions useful in the subject invention formulated as solutions typically include a pharmaceutically-acceptable aqueous or organic solvent. The terms "pharmaceutically-acceptable organic solvent" refer to a solvent which is capable of having the actives dispersed or dissolved therein, and of possessing acceptable safety properties (e.g., irritation and sensitization characteristics). Water is a preferred solvent. Examples of suitable organic solvents include: propylene glycol, polyethylene glycol (200-600), polypropylene glycol (425-2025), glycerol, 1,2,4-butanetriol, sorbitol esters, 1,2,6-hexanetriol, ethanol, isopropanol, sorbitol esters, butanediol, and mixtures thereof. These solutions useful in the subject invention preferably contain from about 80% to about 99.99% of an acceptable aqueous or organic solvent.

If the topical compositions useful in the subject invention are formulated as an aerosol and applied to the skin as a spray-on, a propellant is added to a solution composition. Examples include chloro-fluorinated lower molecular weight hydrocarbons. A more complete disclosure of propellants useful herein can be found in Sagarin, Cosmetics Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972)

Topical compositions useful in the subject invention may be formulated as a solution comprising an emollient. Such compositions preferably contain from about 2% to about 50% of a topical pharmaceutically-acceptable emollient.

As used herein, "emollients" refer to materials used for the prevention or relief of dryness, as well as for the protection of the skin. A wide variety of suitable emollients are known and may be used herein. Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 32-43 (1972), incorporated

herein by reference, contains numerous examples of suitable materials.

A lotion can be made from a solution carrier system. Lotions typically comprise from about 1% to about 20%, preferably from about 5% to about 10%, of an emollient; and from about 50% to about 90%, preferably from about 60% to about 80%, water.

Another type of product that may be formulated from a solution carrier system is a cream. A cream typically comprises from about 5% to about 50%, preferably from about 10% to about 20%, of an emollient, and from about 45% to about 85%, preferably from about 50% to about 75%, water.

Yet another type of product that may be formulated from a solution carrier system is an ointment. An ointment may comprise a simple base of animal or vegetable oils or semi-solid hydrocarbons (oleaginous). Ointments may also comprise absorption ointment bases which absorb water to form emulsions. Ointment carriers may also be water soluble. An ointment may comprise from about 2% to about 10% of an emollient; and from about 0.1% to about 2% of a thickening agent. A more complete disclosure of thickening agents useful herein can be found in Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 72-73 (1972).

If the carrier is formulated as an emulsion, preferably from about 1% to about 10%, more preferably from about 2% to about 5%, of the carrier system comprises an emulsifier. Emulsifiers may be nonionic, anionic or cationic. Suitable emulsifiers are disclosed in, for example, U.S. Patent 3,755,560, issued August 28, 1973, Dickert et al.; U.S. Patent 4,421,769, issued December 20, 1983, Dixon et al.; and McCutcheon's Detergents and Emulsifiers, North American Edition, pages 317-324 (1986);

The cleaning compositions useful in the subject invention preferably contain from about 1% to about 90%, more preferably from about 5% to about 10%, of a cosmetically-acceptable surfactant.

The physical form of the cleansing compositions is not critical. The compositions can be, for example, formulated as toilet bars, liquids, shampoos, pastes, or mousses. Toilet bars are most preferred since this is the form of cleansing agent most commonly used to wash the skin. Rinse-off cleansing compositions, such as shampoos, require a delivery system adequate to deposit sufficient levels of actives on the skin and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure, see U.S. Patent 4, 835,148, Barford et al., issued May 30, 1989; incorporated herein by reference in its entirety.

The cleaning compositions useful in the subject invention can optionally contain, at their art-established levels, materials which are conventionally used in cleansing compositions. Nonlimiting examples of possible surfactants include isoceteth-20, sodium methyl cocoyl taurate, sodium methyl oleoyl taurate, and sodium lauryl sulfate. See U.S. Patent No. 4,800,197, to Kowcz et al., issued January 24, 1989, which is incorporated herein by reference in its entirety. Examples of a broad variety of additional surfactants useful herein are described in McCutcheon's, Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation, which is incorporated herein by reference in its entirety.

Combination Actives

A. Anti-Inflammatory Agents

An anti-inflammatory agent may be included as an active along with the active agents, to reduce the redness and irritation of inflamed acne lesions. A safe and effective amount of an anti-inflammatory agent may be added to the compositions useful in the subject invention, preferably from about 0.1% to about 10%, more preferably from about 0.5% to about 5%, of the composition. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular anti-inflammatory agent utilized since such agents vary widely in potency.

Steroidal anti-inflammatory agents, including but not limited to, corticosteroids such as hydrocortisone, hydroxyltriamcinolone, alpha-methyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionates, clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorisone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclorolone acetonide, fludrocortisone, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylesters, fluocortolone, fluprednidene (fluprednylidene) acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenolone, fludrocortisone, diflurosone diacetate, fluradrenolone acetonide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, chlorprednisone acetate, clocortelone, clescinolone, dichlorisone, diflurprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylpropionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate,

triamcinolone, and mixtures thereof may be used. The preferred steroidal anti--inflammatory for use is hydrocortisone.

A second class of anti-inflammatory agents which is useful in the compositions includes the nonsteroidal anti-inflammatory agents. The variety of compounds encompassed by this group are well-known to those skilled in the art. For detailed disclosure of the chemical structure, synthesis, side effects, etc. of non-steroidal anti-inflammatory agents, reference may be had to standard texts, including Anti-inflammatory and Anti-Rheumatic Drugs, K.D. Rainsford, Vol. I-III, CRC Press, Boca Raton, (1985), and Anti-inflammatory Agents, Chemistry and Pharmacology, 1, R.A. Scherrer, et al., Academic Press, New York (1974).

Specific non-steroidal anti-inflammatory agents useful in the composition invention include, but are not limited to:

1) the oxicams, such as piroxicam, isoxicam, tenoxicam, sudoxicam, and CP-14,304;
2) the acetic acid derivatives, such as diclofenac, fenclofenac, indomethacin, sulindac, tolmetin, isoxepac, furofenac, tiopinac, zidometacin, acematacin, fentiazac, zomepirac, clindanac, oxepinac, felbinac, and ketorolac;
3) the fenamates, such as mefenamic, meclofenamic, flufenamic, niflumic, and tolfenamic acids;
4) the propionic acid derivatives, such as ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indopropfen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, and tiaprofenic; and
5) the pyrazoles, such as phenylbutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone.

Mixtures of these non-steroidal anti-inflammatory agents may also be employed, as well as the pharmaceutically-acceptable salts and esters of these agents. For example, etofenamate, a flufenamic acid derivative, is particularly useful for topical application. Of the nonsteroidal anti-inflammatory agents, ibuprofen, naproxen, flufenamic acid, mefenamic acid, meclofenamic acid, piroxicam and felbinac are preferred; ibuprofen, naproxen, and flufenamic acid are most preferred.

Finally, so-called "natural" anti-inflammatory agents are useful in methods of the subject invention. For example, candelilla wax, alpha bisabolol, aloe vera, Manjistha (extracted from plants in the genus Rubia, particularly Rubia Cordifolia), and Guggal (extracted from plants in the genus Commiphora,

particularly Commiphora Mukul), may be used.

B. Retinoids

In a preferred composition useful in the subject invention, a retinoid, preferably retinoic acid, is included as an active along with the active agents. The inclusion of a retinoid increases the anti-acne benefits of the composition and suppresses sebum production in the skin. A safe and effective amount of a retinoid may be added to the compositions useful in the subject invention, preferably from about 0.001% to about 0.5%, more preferably from about 0.01% to about 0.1% of the composition. As used herein, "retinoid" includes all natural and/or synthetic analogs of Vitamin A or retinol-like compounds which possess the biological activity of Vitamin A in the skin as well as the geometric isomers and stereoisomers of these compounds, such as all-trans retinoic acid and 13-cis-retinoic acid.

C. Antiandrogens

In a preferred composition useful in the subject invention, an antiandrogen is included as an active along with the active agents. As used herein, "anti-androgen" means a compound capable of correcting androgen-related disorders by interfering with the action of androgens at their target organs. The target organ for the subject invention is mammalian skin. Preferred antiandrogens include cyproterone thiopivalate and cyproterone acetate thioacetate.

D. Glycolic Acid

In a preferred composition of the subject invention, glycolic acid is included as an active along with the subject anti-acne agents. Preferably, the composition comprises from about 0.1% to about 10%; more preferably from about 1% to about 6%, also preferably from about 2% to about 5% glycolic acid.

E. Anti-acne Agents

In a preferred composition of the subject invention, an additional anti-acne agent is included as an active along with the subject anti-acne agents. Preferred additional anti-acne agents include hesperetin and phloretin. Preferably, the composition comprises from about 0.1% to about 5%, more preferably about 0.5% to about 3%, also preferably from about 1% to about 2% of an anti-acne agent.

Delivery Methods for the Topical Compositions

The topical compositions useful for the methods of the instant invention can be delivered from a variety of delivery devices. The following are two nonlimiting examples.

Medicated Cleansing Pads

The compositions useful herein can be incorporated into a medicated cleansing pad. Preferably these pads comprise from about 50% to about 75% by weight of one or more layers of nonwoven fabric material and from about 20% to about 50% by weight of a liquid composition deliverable from the nonwoven fabric material comprising hydroxy acid comprising salicylic acid and a subject zwitterionic surfactant, or mixture of such surfactants. These pads are described in detail in U. S. Patent No. 4,891,228, to Thaman et al., issued January 2, 1990; and U. S. Patent No. 4,891,227, to Thaman et al., issued January 2, 1990; both of which are incorporated by reference herein in their entirety.

Dispensing Devices

The compositions useful herein can also be incorporated into and delivered from a soft-tipped or flexible dispensing device. These devices are useful for the controlled delivery of the compositions to the skin surface and have the advantage that the treatment composition itself never need be directly handled by the user. Nonlimiting examples of these devices comprise a fluid container including a mouth, an applicator, means for holding the applicator in the mouth of the container, and a normally closed pressure-responsive valve for permitting the flow of fluid from the container to the applicator upon the application of pressure to the valve. The fluid comprises hydroxy acid comprising salicylic acid and a subject zwitterionic surfactant, or mixture of such surfactants.

The valve can include a diaphragm formed from an elastically fluid impermeable material with a plurality of non-intersecting arcuate slits therein, where each slit has a base which is intersected by at least one other slit, and where each slit is out of intersecting relation with its own base, and wherein there is a means for disposing the valve in the container inside of the applicator. Examples of these applicator devices are described in U.S. Patent No. 4,693,623, to Schwartzman, issued September 15, 1987; U.S. Patent No. 4,620,648, to Schwartzman, issued September 15, 1987; U.S. Patent No. 3,669,323, to Harker et al., issued June 13, 1972; U.S. Patent No. 3,418,055, to Schwartzman, issued December 24, 1968; and U.S. Patent No. 3,410,645, to Schwartzman, issued November 12, 1968; all of which are incorporated herein by reference in their entirety. Examples of applicators useful herein are commercially available from Dab-O-Matic, Mount Vernon, NY.

METHODS FOR TREATMENT OF ACNE

The subject invention relates to methods of treating acne in mammalian skin. Such methods comprise topically applying to the skin or scalp an effective amount of the compositions of the subject invention. The term "effective

amount", as used herein, means an amount sufficient to provide an anti-acne benefit. The composition can be applied for several days, weeks, months or years at appropriate intervals: from about three times a day to about once every three days, preferably from about twice a day to once every other day, also preferably about once a day until a satisfactory anti-acne benefit has been achieved.

Typically, in each application, an effective coating of the skin or scalp is achieved by applying from about 0.004mg/cm^2 to about 0.1 mg/cm^2 each of benzoyl peroxide and a subject zwitterionic surfactant, or mixture of such surfactants, more preferably from about 0.02mg/cm^2 to about 0.06mg/cm^2 of each agent, also preferably about 0.04 mg/cm^2 of each agent.

Examples

The following examples further describe and demonstrate embodiments within the scope of the subject invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the subject invention, as many variations thereof are possible without departing from the spirit and scope of the invention.

Example I

A topical composition is prepared by combining the following components utilizing conventional mixing techniques.

Ingredient	% Weight
Water	50.67
Triethanolamine	0.66
Cetyl Betaine	6.66
Disodium EDTA	0.01
Ethanol (95%)	32.00
Benzoyl Peroxide	10.00

The above composition is applied to the face to treat acne at a dose enough to deposit 2 mg of the composition per cm^2 skin, once a day. As existing acne subsides, application is reduced to once every other day.

Example II

A cleaning composition is prepared by combining the following ingredients, using conventional mixing techniques:

Ingredient	% Weight
Water	44.75
Tetrasodium EDTA	0.12
Cetyl Betaine	3.33
Sodium methyl cocoyl taurate	41.67

Cetyl propyl hydroxysultaine	6.00
Benzoyl peroxide	2.00
Cocoamidopropyl betaine	1.43
Hydroxypropyl methylcellulose	0.50
Glycolic Acid	0.20
Perfume	0.12

The cleaning composition is applied to the face twice a day to treat acne. An amount enough to deposit 3 mg of the composition per cm^2 skin is used. As existant acne subsides, frequency is reduced to once a day.

Example III

The following topical gel is prepared by mixing the ingredients according to conventional mixing techniques:

Ingredients	% Weight
Alcohol SD-40 (95%)	40.00
Benzoyl peroxide	2.00
Disodium EDTA	0.005
Cetyl Betaine	6.66
Water	47.335

The gel is applied to the face at a dose of 0.2 mg composition per cm^2 skin three times a day to treat acne. As treatment progresses, application is reduced to once a day.

Example IV

The following lotion is prepared by mixing the ingredients according to conventional mixing techniques:

Ingredient	% Weight
Water	69.96
Glycerin	10.
Petrolatum	2.5
Cetyl Alcohol	1.8
Cyclomethicone and Dimethicone Copolyol	1.5
Stearyl Alcohol	1.2
Isopropyl Palmitate	1.0
Dimethicone	0.5
Sodium Hydroxide	0.34
Lanolin Acid	0.25
Polyethyleneglycol-100 Stearate	0.25

Stearic Acid	0.25
Methylparaben	0.2
Titanium Dioxide	0.15
EDTA	0.1
Benzoyl peroxide	5.0
Cocoamidopropyl Betaine	5.0

The above lotion is applied to the face once a day at a dose of .75 mg composition per cm^2 skin. As existant acne subsides, frequency of application is reduced to once every two days.

EXAMPLE V

The following cleaning solution is prepared by mixing the ingredients according to conventional mixing techniques:

Ingredient	% Weight
Water	85.3
Carbopol 980	.9
Cetyl betaine	2.0
EDTA disodium	.1
NaOH solution (5%)	9.2
Benzoyl Peroxide	2.5

The above lotion is applied to the face twice a day at a dose of .90 mg composition per cm^2 skin. As existant acne subsides, frequency of application is reduced to once a day.

EXAMPLE VI

The following lotion is prepared by mixing the ingredients according to conventional mixing techniques:

Ingredient	% Weight
Carbopol 980	.9
Water	80.5
EDTA disodium	0.1
Cetyl betaine	2.0
Dow Corning Anti Foam	1.0
Cetyl Alcohol	1.5
Stearyl Alcohol	1.5
Steareth-2[1]	.9
Steareth-21[1]	.1
Benzoyl Peroxide	2.5
Cyclomethicone D4/D5	.5
NaOH solution (5%)	8.5

[1]obtained from ICI Americas

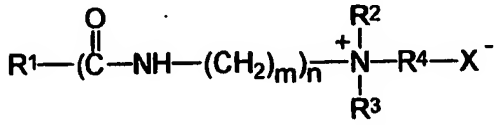
The above lotion is applied to the face once every other day at a dose of 20 mg composition per cm^2 skin. As existant acne subsides, frequency of application is reduced to once a week.

While particular embodiments of the subject invention have been described, it will be obvious to those skilled in the art that various changes and modifications to the subject invention can be made without departing from the spirit and scope of the invention. It is intended to cover, in the appended claims, all such modifications that are within the scope of the subject invention.

What is Claimed is:

1. An anti-acne composition useful for topical application characterized in that it comprises:

a) a safe and effective amount of zwitterionic surfactant having the structure:



wherein R^1 is unsubstituted, saturated or unsaturated, straight or branched chain alkyl having from 9 to 22 carbon atoms; m is an integer from 1 to 3; n is 0 or 1; R^2 and R^3 are, independently, saturated, straight chained alkyl having from 1 to 3 carbon atoms, unsubstituted or mono-substituted with hydroxy; R^4 is saturated or unsaturated, straight or branched chain alkylene, unsubstituted or mono-substituted with hydroxy, having from 1 to 5 carbon atoms; and X is selected from the group consisting of CO_2, SO_3 and SO_4;

b) a safe and effective amount of benzoyl peroxide; and

c) a topical carrier.

2. A composition according to Claim 1 wherein:

(a) the concentration of benzoyl peroxide is from 0.1% to 10%; and

(b) the concentration of zwitterionic surfactant is from 0.1% to 10%.

3. A composition according to any preceding claim wherein:

(a) R^2 and R^3 is CH_3, CH_2CH_2OH, $CH_2CH_2CH_2OH$;

(b) X is CO_2 or SO_3; and

(c) m is 2 or 3.

4. A composition according to Claim 3 wherein R^4 is saturated, straight chained, and has from 1 to 3 carbon atoms when X is CO_2, and from 2 to 4 carbon atoms when X is SO_3.

5. A composition according to Claim 4 wherein:

a) R^1 is a saturated, straight chain alkyl with from 11 to 18 carbon atoms;

b) R^2 and R^3 are CH_3; and

c) R^4 has 1 carbon atom when X is CO_2; and R^4 has 3 carbon atoms when X is SO_3.

d) m is 3; and

e) n is 1.

6. The composition of any preceding claim wherein:

(a) the concentration of benzoyl peroxide is from 1% to 6%; and

(b) the concentration of zwitterionic surfactant is from 1% to 6%.

7. A composition of any preceding claim wherein the composition further comprises from 1% to 6% of glycolic acid.

8. A composition according to any preceding claim wherein the zwitterionic surfactant is behenyl betaine, cocoamidopropyl betaine, cetyl propyl hydroxy sultaine or cetyl betaine.

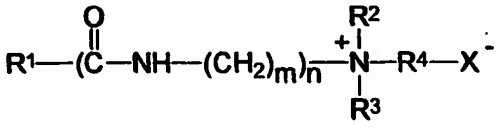
9. A composition according to any of the proceeding claims wherein;

(a) the amount of benzoyl peroxide when applied topically is from 0.004 mg/cm^2 skin to 0.1 mg/cm^2 skin; and

(b) the amount of zwitterionic surfactant when applied topically is from 0.004 mg/cm^2 skin to 0.1 mg/cm^2 skin.

10. The use of components for the preparation of a topical anti-acne composition according to claim 1 characterized in that the components comprise;

a) a safe and effective amount of zwitterionic surfactant having the structure:



wherein R^1 is unsubstituted, saturated or unsaturated, straight or branched chain alkyl having from 9 to 22 carbon atoms; m is an

integer from 1 to 3; n is 0 or 1; R^2 and R^3 are, independently, saturated, straight chained alkyl having from 1 to 3 carbon atoms, unsubstituted or mono-substituted with hydroxy; R^4 is saturated or unsaturated, straight or branched chain alkylene, unsubstituted or mono-substituted with hydroxy, having from 1 to 5 carbon atoms; and X is selected from the group consisting of CO_2, SO_3 and SO_4;

b) a safe and effective amount of benzoyl peroxide; and

c) a topical carrier.

INTERNATIONAL SEARCH REPORT

Intern. al Application No
PCT/US 95/02489

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LU,A,68 215 (FLOW PHARMACEUTICALS INC.) 21 February 1974 see the whole document ---	1-10
A	EP,A,0 335 115 (L'OREAL) 4 October 1989 see the whole document ---	1-10
A	EP,A,0 413 528 (YU RUEY J.) 20 February 1991 see the whole document ---	1-10
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A	WO,A,90 00899 (CIRO'S TOUCH LTD) 8 February 1990 see the whole document ---	1-10
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 July 1995	07.08.95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Couckuyt, P

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INTERNATIONAL SEARCH REPORT

Intern. al Application No
PCT/US 95/02489

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A,4 228 163 (BLISS) 14 October 1980 see the whole document	1-10
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